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RAC Application for FHCRC Protocol 1503
" A Phase I Study to Evaluate the Safety of Cellular Immunotherapy using genetically-modified Autologous CD20-specific CDS+ T cell Clones for Patients with relapsed CD20+ Indolent Lymphomas"

Scientific Abstract

More than 55,000 new cases of non-Hodgkin's lymphoma are diagnosed each year in the United States and recent epidemiological data demonstrates that the incidence of this disease is increasing. Follicular non-Hodgkin's lymphoma (FL) is one of the most common sub-types of NHL, accounting for 20-30% of all cases and nearly 85% of FL patients have widespread (stage III-IV) disease at the time of diagnosis. No curative treatment is available for advanced follicular lymphomas, with the possible exception of high dose chemoradiotherapy with stem cell transplantation. However, most patients who develop follicular lymphomas are elderly and are not suitable candidates for aggressive stem cell transplantation protocols. Innovative new treatments are therefore needed. This protocol proposes to examine the safety of administering autologous ex-vivo expanded $CD8^+$ cytotoxic T lymphocyte (CTL) clones genetically modified to express a CD20-specific chimeric immunoreceptor (scFvFc:ζ) as a novel new treatment for patients with relapsed FL. Peripheral blood mononuclear cells (PBMC) isolated from study subjects will be genetically modified by electroporation with a plasmid DNA construct encoding the scFvFc:ζ under the transcriptional control of the CMV immediate/early promoter. These genetically modified T cells will be cloned and expanded to large numbers outside the body for subsequent re-infusion. Twenty-eight days following completion of six cycles of cytoreductive chemotherapy with CVP (cyclophosphamide, vincristine and prednisone), patients will receive a series of three infusions of their genetically modified CD20-specific $CD8^+$ CTL clones at 2 week intervals. Each patient will be evaluated to establish the safety of this procedure by infusing $1x10^8$ cells/m^2 on the first week, followed by $1x10^9$ cells/m^2 two weeks later and finally $3.3\ x10^9$ cells/m^2 two weeks after the second infusion. Six of the twelve planned patients will also receive treatment with low dose subcutaneous interleukin 2 for 60 days to maintain the CTL in vivo. The secondary objectives of this protocol are to study the *in vivo* persistence of transferred cells and to document the trafficking of transferred cells to lymph nodes. The anti-lymphoma activity of infused clones will be assessed by standard radiographic and clinical follow-up as well as by fluorodeoxyglucose-positron emission tomography (FDG-PET). Additionally, peripheral blood samples will be obtained following adoptive therapy and evaluated for evidence of humoral and cellular immune reactivity against the infused genetically modified clones.